OPEN ACCESS

Greenfort International Journal of Applied Medical Science

Abbreviated Key Title: Grn Int J Apl Med Sci | ISSN 3048-6904(P) | ISSN 2584-2420(O) |
Greenfort International Publisher, Assam, India
Journal homepage: https://gijams.in

Research Article DOI: 10.62046/gijams.2025.v03i02.008

Effects of Nicotine withdrawal on the Plasma Lipid Profile of Wistar Rats fed with High-fat diet

Onyebuchi Obia[1], Ledu Nda-ue[2], Frank Nwabueze Nwokocha[2]

[1]Department of Human Physiology, faculty of Basic Medical Sciences, College of Medical Sciences, Rivers State University, Nkpolu-Oroworukwo, Port Harcourt, Nigeria.
[2]Department of Human Physiology, faculty of Basic Medical Sciences, College of Health Sciences, University of Port Harcourt, Nigeria.

***Corresponding Author:** Onyebuchi Obia | **Received:** 01.02.2025 | **Accepted:** 14.03.2025 | **Published:** 24.03.2025

Abstract: **Background to the study**: Nicotine is the main active component of cigarettes. Smoking has been associated with higher prevalence of abnormalities in lipid metabolism. This study investigated the effects of nicotine withdrawal on the plasma lipid profile of wistar rats fed with high-fat diet (HFD). **Methodology**: The experiment involved 24 male wistar rats separated into 3 groups of 8 rats each. All the animals were placed on high-fat diet in addition to their respective doses of nicotine as follows; Groups 1, 2 and 3 received 200µg/kg, 400µg/kg and 800µg/kg of nicotine oral solution respectively. The experiment was performed in two phases. In the first phase, the animal groups were placed on their respective doses of nicotine solution for 4 weeks. Thereafter, 4 animals in each group were sacrificed and blood samples collected to determine their nicotine exposed plasma lipid profile. In the second phase of the experiment, nicotine was discontinued in all the groups. The remaining 4 animals in each group continued without nicotine for the next four weeks after which they were sacrificed and blood samples collected to determine their nicotine withdrawal plasma lipid profile. **Results**: The results showed that the levels of total cholesterol (TC), high-density lipoprotein (HDL) and low-density lipoprotein (LDL) increased significantly while there was no significant change in triglycerides (TG) concentration four weeks after withdrawal of 200µg of nicotine compared to the exposed groups. However, following cessation of 400µg and 800µg respectively of nicotine, the plasma levels of TC, TG, HDL and LDL increased significantly compared to their exposed groups suggestive of an initial suppression of the lipid profile parameters with nicotine exposure. **Conclusion**: Conclusively, higher concentrations of nicotine caused significant suppression of TC, TG, HDL and LDL with significant reversal in the four weeks preceding exposure. Therefore, in quitting smoking, it is important to reduce or stop the consumption of high-fat diet in the immediate periods following cessation of nicotine. The study also recommends that nicotine cessation programs should be accompanied by improved physical activity to prevent possible post-cessation excessive weight gain.

Keywords: Nicotine, withdrawal, Plasma lipid profile, high-fat diet, wistar rats.

Citation: Onyebuchi Obia *et al*. Effects of Nicotine withdrawal on the Plasma Lipid Profile of Wistar Rats fed with High-fat diet. Grn Int J Apl Med Sci, 2025 Mar-Apr 3(2): 70-73.

INTRODUCTION

The growing number of retail food outlets which prepare meals enriched with high levels of fats is a public health concern and may be contributory to the rising prevalence of obesity and dyslipidaemia [1-4]. Smoking and obesity are known risk factors for many cardio-metabolic diseases [5-10]. Although, the smoke from combustible tobacco products contains several chemicals, nicotine is its main active component [11]. It is known to be highly addictive making it almost difficult for cigarette smokers to quit despite having knowledge of its deleterious effects. A higher prevalence of abnormalities in the lipid profile of smokers has been documented in human studies [12-13]. Nicotine particularly increases the plasma triglyceride concentrations while reducing the high density lipoprotein levels. Previous studies have linked exposure to nicotine with a rise in insulin and reduction in blood glucose [14].

Cessation of nicotine is associated with uncomfortable withdrawal symptoms that may compel smokers who wish to quit resuming again. Quitting smoking at an earlier age or after a short period of exposure to cigarette smoke have been associated with lower risk of diseases [15]. The mortality associated with continued smoking might be reduced by about 90% if cessation of smoking occurred before the age of 40 years [16]. The

aim of the present study was to investigate the effects of nicotine withdrawal on the plasma lipid profile [total cholesterol (TC), triglyceride (TG), high-density lipoprotein (HDL) and low-density lipoprotein (LDL)] of wistar rats fed with high-fat diet.

MATERIALS AND METHODS

This study was carried out in the department of Human Physiology, Faculty of Basic Medical Sciences, College of Health Sciences, University of Port Harcourt with ethical approval number: UPH/CEREMAD/REC/MM68/053. The experiment involved 24 male wistar rats separated into 3 groups of 8 rats each which were acclimatized for a period of two weeks being provided with standard animal chow and water *ad libitum*. After acclimatization, all the animals were placed on high-fat diet in addition to the different doses of nicotine in the experimental groups. Groups 1, 2 and 3 received 200µg/kg, 400µg/kg and 800µg/kg of nicotine oral solution respectively. The experiment was performed in two phases. In the first phase, the experimental groups were placed on their respective doses of nicotine solution for 4 weeks. Thereafter, 4 animals in each group were sacrificed and blood samples collected to determine their nicotine exposed plasma lipid profile. In the second phase of the experiment, nicotine was discontinued in all the groups. The remaining 4 animals in each group continued without nicotine for the next four weeks after which they were sacrificed and blood samples collected to determine their nicotine withdrawal plasma lipid profile. All the parameters were determined using standard methods and values recorded.

Data were analyzed using SPSS vs 23 and presented in Tables. Continuous variables were expressed as mean ± SEM. The differences between each group were analyzed using paired sample t-test and ANOVA. Values of $p< 0.05$ were considered significant with a confidence level of 95%.

RESULTS AND DISCUSSION

Table-1: Plasma lipid profile following nicotine exposure and withdrawal in high-fat diet fed wistar rats (mean values are in mmol/l)

Group	Total Cholesterol		Triglyceride		High-density lipoprotein		Low-density lipoprotein	
	Exposure	Withdrawal	Exposure	Withdrawal	Exposure	Withdrawal	Exposure	Withdrawal
200µg	1.80±0.26	4.30±0.08[c]	0.98±0.23	0.98±0.05	0.68±0.16	1.28±0.19[c]	0.88±0.10	2.68±0.13[c]
400µg	2.03±0.10	5.35±0.19[d]	0.50±0.00	1.10±0.07[d]	0.70±0.23	1.95±0.06[d]	0.98±0.14	2.93±0.22[d]
800µg	1.15±0.19	7.98±0.46[e]	0.63±0.22	2.10±0.08[e]	0.28±0.11	1.65±0.16[e]	0.60±0.06	5.43±0.50[e]

c; Significantly higher than exposure group in the 200µg nicotine group.
d; Significantly higher than exposure group in the 400µg nicotine group.
e; Significantly higher than exposure group in the 800µg nicotine group.

In the present study, the levels of total cholesterol (TC), high-density lipoprotein (HDL) and low-density lipoprotein (LDL) increased significantly four weeks after withdrawal of 200µg of nicotine compared to the exposed groups. There was no significant change in the triglycerides (TG) concentration. Following cessation of 400µg and 800µg respectively of nicotine, the plasma levels of TC, TG, HDL and LDL increased significantly compared to their exposed groups. High-fat diet feeding disrupts lipid metabolism increasing the plasma concentrations of TC, TG and LDL and decreased HDL [17]. In the first phase of the study, the levels of lipid profile parameters were probably suppressed by nicotine when administered concomitantly with high-fat diet [18]. In previous studies involving plant extracts, lipid lowering potential is beneficial [19,20]. However, nicotine exposure in animal models have been associated with reduction in body weight, liver weight and blood glucose [18, 21, 14]. These effects could reverse four weeks after the nicotine exposure [14]. Amongst other factors, nicotine suppresses body weight via increased fat metabolism [22] and increased physical activity in animal models [23]. Studies suggest a positive relationship between plasma lipids and blood glucose [24] such that a reduction in the blood glucose could be linked with reduction in the lipid profile parameters. Other studies suggest that nicotine exposure may influence leptin release and therefore cause reduction in food intake and alteration in energy expenditure amongst smokers [25-27]. The results from our study in high-fat diet fed wistar rats did not agree with previous studies on human smokers where nicotine increased the levels of TC, TG and LDL but reduce the concentrations of HDL compared to non-smokers [28].

Cessation of nicotine is commonly associated with some unpleasant effects which are more pronounced within the first week post-exposure [29]. In our study, using high-fat diet fed wistar rats, the withdrawal of nicotine for a period of 4 weeks after initial 4-week exposure resulted in an increase in the lipid profile parameters (TC, TG, HDL and LDL) compared to the nicotine exposed groups. Cessation of nicotine improves food intake and reduces nicotine-induced increased metabolic rate [30] leading to weight gain [31,32]. The beneficial effects of smoking cessation may be obscured by weight gain in the periods following cessation. This underscores the need to add regimens such as improved physical activity and dietary

modifications in smoking cessation program [33]. In our study, the increase in LDL levels 4 weeks after nicotine cessation could suggest that in the preceding initial weeks after quitting smoking, the risk of cholesterol induced morbidity and mortality might still be unaltered. A similar study in human subjects showed that smoking cessation did not affect the concentration of LDL [31]. This result differs from our study in which high-fat diet (HFD) was continuously being administered after nicotine cessation. However, the post-nicotine rise in HDL may be part of reduced cardiovascular risk associated with nicotine cessation.

Conclusively, higher concentrations of nicotine caused significant suppression of TC, TG, HDL and LDL with a reversal in the four weeks preceding exposure. Therefore, in quitting smoking, it is important to reduce or stop the consumption of high-fat diet in the immediate periods following cessation of nicotine.

REFERENCES

1. **Smith**, D., Cummins, S., Clark, C., & Stansfeld, S. (2013). Does the local food environment around schools affect diet? Longitudinal associations in adolescents attending secondary schools in East London. *BMC public health*, *13*, 70. https://doi.org/10.1186/1471-2458-13-70
2. **da** Costa Peres, C. M., Gardone, D. S., Costa, B. V. L., Duarte, C. K., Pessoa, M. C., & Mendes, L. L. (2020). Retail food environment around schools and overweight: a systematic review. *Nutrition reviews*, *78*(10), 841–856. https://doi.org/10.1093/nutrit/nuz110
3. **Li**, J., Wu, H., Liu, Y., & Yang, L. (2020). High fat diet induced obesity model using four strainsof mice: Kunming, C57BL/6, BALB/c and ICR. *Experimental animals*, *69*(3), 326–335. https://doi.org/10.1538/expanim.19-0148
4. **de** Albuquerque, F. M., Pessoa, M. C., De Santis Filgueiras, M., Gardone, D. S., & de Novaes, J. F. (2022). Retail food outlets and metabolic syndrome: a systematic review of longitudinal studies. *Nutrition reviews*, *80*(6), 1599–1618. https://doi.org/10.1093/nutrit/nuab111
5. **Santos**, A. C., Lopes, C., Guimarães, J. T., & Barros, H. (2005). Central obesity as a major determinant of increased high-sensitivity C-reactive protein in metabolic syndrome. *International journal of obesity*, 29(12), 1452–1456. https://doi.org/10.1038/sj.ijo.0803035
6. **Nwafor**, A., Mmom, F., Obia, O., Obiandu, C., Hart, V. O., & Chinko, B. C. (2015). Relationship Between Blood Pressure, BloodGlucose And Body Mass Index And Coexisting Prehypertension And Prediabetes Among Rural Adults In Niger Delta Region,Nigeria. *British Journal of Medicine and Medical Research*. 9 (7), 1-12.
7. **Maddatu**, J., Anderson-Baucum, E., & Evans-Molina, C. (2017). Smoking and the risk of type 2 diabetes. *Translational research: the journal of laboratory and clinical medicine*, *184*, 101–107. https://doi.org/10.1016/j.trsl.2017.02.004
8. **Kondo**, T., Nakano, Y., Adachi, S., & Murohara, T. (2019). Effects of Tobacco Smoking on Cardiovascular Disease. *Circulation journal: official journal of the Japanese Circulation Society*, 83(10), 1980–1985.
9. **Parmar**, M. P., Kaur, M., Bhavanam, S., Mulaka, G. S. R., Ishfaq, L., Vempati, R., C, M. F., Kandepi, H. V., Er, R., Sahu, S., & Davalgi, S. (2023). A Systematic Review of the Effects of Smoking on the Cardiovascular System and General Health. *Cureus*, 15(4), e38073. https://doi.org/10.7759/cureus.38073
10. **Hu**, H., Nakagawa, T., Honda, T., Yamamoto, S., & Mizoue, T. (2024). Association of conventional cigarette smoking, heated tobacco product use and dual use with hypertension. *International journal of epidemiology*, 53(5), dyae114. https://doi.org/10.1093/ije/dyae114
11. **Sansone**, L., Milani, F., Fabrizi, R., Belli, M., Cristina, M., Zagà, V., de Iure, A., Cicconi, L., Bonassi, S., & Russo, P. (2023). Nicotine: From Discovery to Biological Effects. *International journal of molecular sciences*, *24*(19), 14570. https://doi.org/10.3390/ijms241914570
12. **Hasan**, H., Arhouma, T., Khanfar, M., & Azzam, M. (2022) Study the Relationship between the Nicotine and Lipid Profile with Some Hematology Parameters in Serum of Smoker and Non-Smoker Blood Samples. *Journal of Biosciences and Medicines*, **10**, 20-36. doi: 10.4236/jbm.2022.106003.
13. **Momayyezi**, M., Jambarsang, S., Fallahzadeh, H., & Sefidkar, R. (2024). Association between lipid profiles and cigarette smoke among adults in the Persian cohort (Shahedieh) study. *BMC Public Health* **24**, 1256. https://doi.org/10.1186/s12889-024-18734-0
14. **Obia,** O., Nda-ue, L., Ojeka, S. O., Ogba, A., & Nwokocha, F. N. (2024). Impact of Nicotine Exposure and Withdrawal on Plasma Glucose, Insulin and Glycated Hemoglobin in High-fat diet fed Wistar Rats. *East African Scholars Journal of Medical Sciences*. 7(4), 138-143.
15. **Cho**, E. R., Brill, I. K., Gram, I. T., Brown, P. E., & Jha, P. (2024). Smoking Cessation and Short- and Longer-Term Mortality. *NEJM evidence*, *3*(3), EVIDoa2300272. https://doi.org/10.1056/EVIDoa2300272
16. **Jha**, P., Ramasundarahettige, C., Landsman, V., Rostron, B., Thun, M., Anderson, R. N., McAfee, T., & Peto, R. (2013). 21st-century hazards of smoking and benefits of cessation in the United States. *The New England journal of medicine*, *368*(4), 341–350. https://doi.org/10.1056/NEJMsa1211128
17. **Binayi**, F., Moslemi, M., Khodagholi, F., Hedayati, M., & Zardooz, H. (2020). Long-term high-fat diet

disrupts lipid metabolism and causes inflammation in adult male rats: possible intervention of endoplasmic reticulum stress. *Archives of Physiology and Biochemistry*, *129*(1), 204–212. https://doi.org/10.1080/13813455.2020.1808997

18. **Wang**, R., Li, S., Jin, L., Zhang, W., Liu, N., Wang, H., Wang, Z., Wei, P., Li, F., Yu, J., Lu, S., Chen, Y., Li, Z., & Wu, C. (2019). Four-week administration of nicotinemoderately impacts blood metabolic profile and gut microbiota in a diet-dependent manner, *Biomedicine & Pharmacotherapy*, 115, 108945.
19. **Emmanuel**, F. D., Obia, O., Charles, C., Okari, K. A., Otto, J. B., Reuben, E., & Onyeso, G. (2025). Comparative Assessment of Red, Green and Black pepper species on Plasma and Fecal Lipid Profile of High-fat diet fed wistar rats. *International Journal of Biochemistry Research & Review*, 34(1), 153 163.
20. **Obia,** O., Kalio, R. O., Tee, P. G. P., & Onyeso, G. (2025). Plasma Lipid Lowering Potential of Carrot (Daucus carota) Extract in Male Wistar Rats. *Asian Journal of Research in Medical and Pharmaceutical Sciences*, 14(1), 18-23.
21. **Dangana**, E. O., Omolekulo, T. E., Areola, E. D., Olaniyi, K. S., Soladoye, A. O., & Olatunji, L. A. (2020). Sodium acetate protects against nicotine-induced excess hepatic lipid in male rats by suppressing xanthine oxidase activity. *Chemico-biological interactions*, *316*, 108929. https://doi.org/10.1016/j.cbi.2019.108929
22. **Rupprecht**, L. E., Kreisler, A. D., Spierling, S. R., de Guglielmo, G., Kallupi, M., George, O., Donny, E. C., Zorrilla, E. P., & Sved, A. F. (2018). Self-administered nicotine increases fat metabolism and suppresses weight gain in male rats. *Psychopharmacology*, 235(4), 1131–1140.
23. **Liu**, M., Chuang Key, C. C., Weckerle, A., Boudyguina, E., Sawyer, J. K., Gebre, A. K., Spoo, W., Makwana, O., & Parks, J. S. (2018). Feeding of tobacco blend or nicotine induced weight loss associated with decreased adipocyte size and increased physical activity in male mice. *Food and chemical toxicology: an international journal published for the British Industrial Biological Research Association*, 113, 287–295. https://doi.org/10.1016/j.fct.2018.01.058
24. **Wang**, L., Yan, N., Zhang, M., Pan, R., Dang, Y., & Niu, Y. (2022). The association between blood glucose levels and lipids or lipid ratios in type 2 diabetes patients: A cross-sectional study. *Frontiers in endocrinology*, 13, 969080. https://doi.org/10.3389/fendo.2022.969080
25. **Bellinger**, L. L., Wellman, P. J., Harris, R. B., Kelso, E. W., & Kramer, P. R. (2010). The effects of chronic nicotine on meal patterns, food intake, metabolism and body weight of male rats. *Pharmacology, biochemistry, and behavior*, 95(1), 92–99. https://doi.org/10.1016/j.pbb.2009.12.012
26. **Suhaimi**, M. Z., Sanip, Z., Jan, H. J., & Yusoff, H. M. (2016). Leptin and calorie intake among different nicotine dependent groups. *Annals of Saudi medicine*, 36(6), 404–408. https://doi.org/10.5144/0256-4947.2016.404
27. **Calarco**, C. A., & Picciotto, M. R. (2020). Nicotinic Acetylcholine Receptor Signaling in the Hypothalamus: Mechanisms Related to Nicotine's Effects on Food Intake. *Nicotine & tobacco research: official journal of the Society for Research on Nicotine and Tobacco*, *22*(2), 152–163. https://doi.org/10.1093/ntr/ntz010
28. **Nath,** M. C., Rahman, A. K. M. S., Nath, M. C., Dutta, A., Khan, Z. H., Ghosh, E., Akhter, S., Islam, M. S., Sultana, S., Begum, R., & Rahman, M. M. (2022). The Effect of Cigarette Smoking on Fasting Lipid Profile: A Single Center Study. *Fortune Journal of Health Sciences*, 5(2): 363-373.
29. **Chellian**, R., Behnood-Rod, A., Bruijnzeel, D. M., Wilson, R., Pandy, V., & Bruijnzeel, A. W. (2021). Rodent models for nicotine withdrawal. *Journal of psychopharmacology (Oxford, England)*, *35*(10), 1169–1187. https://doi.org/10.1177/02698811211005629
30. **Liakoni**, E., Edwards, K. C., St Helen, G., Nardone, N., Dempsey, D. A., Tyndale, R. F., & Benowitz, N. L. (2019). Effects of Nicotine Metabolic Rate on Withdrawal Symptoms and Response to Cigarette Smoking After Abstinence. *Clinical pharmacology and therapeutics*, *105*(3), 641–651. https://doi.org/10.1002/cpt.1238
31. **Gepner**, A. D., Piper, M. E., Johnson, H. M., Fiore, M. C., Baker, T. B., & Stein, J. H. (2011). Effects of smoking and smoking cessation on lipids and lipoproteins: outcomes from a randomized clinical trial. *American heart journal*, *161*(1), 145–151. https://doi.org/10.1016/j.ahj.2010.09.023
32. **Driva**, S., Korkontzelou, A., Tonstad, S., Tentolouris, N., & Katsaounou, P. (2022). The Effect of Smoking Cessation on Body Weight and Other Metabolic Parameters with Focus on People with Type 2 Diabetes Mellitus. *International journal of environmental research and public health*, *19*(20), 13222. https://doi.org/10.3390/ijerph192013222
33. **Obia**, O., Efone, P. E., & Wichendu, P. N. (2015). Effect of Exercise on the Blood Pressure of Cigarette Smokers. *The International journal of innovative research and development*, 4 (8), 88–90.